Amendments to the Drawings

Applicants respectfully propose an amendment to Figure 4A as shown in the enclosed replacement pages to correct a typographical error in element numbering. Entry of the proposed amendment to the drawings is respectfully requested.

Remarks

Reconsideration and withdrawal of the rejections set forth in the Office action dated November 3, 2005 are respectfully requested. Applicants petition the Commissioner for a 3-month extension of time. A separate petition accompanies this amendment.

Claims 1-38 are pending. Claims 5, 8-10, 12, 14, 22-24, 27-28, 32-34, and 36-38 are withdrawn. Claims 39-81 are canceled. Claims 1-4, 6-7, 11, 13, 15-21, 25-26, 29-31, and 35 are under examination.

I. Amendments

The specification is amended to remove embedded hyperlinks.

The specification is further amended to correct obvious typographical errors.

Figure 4A is amended to change "82" to "72."

Claims 9-10, 28, 33-34, and 38 are withdrawn. Upon allowance of the generic claims, Applicants request consideration of claims to additional species which are written in dependent form or which otherwise include all the limitations of the allowed generic claim(s) as provided by 37 C.F.R. §1.141.

Claim 7 is amended to clarify the sequences.

No new matter is added by way of these amendments.

II. Election/Restriction

In the Office Action, claims 5, 7, 8, 9-10, 12, 14-15, 22-24, 27-28, 32-34, and 36-38 were withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b) as allegedly being drawn to nonelected species. Applicants respectfully submit that claims 7 and 15 read on the elected species.

Specifically, claim 7 recites that the first and third polypeptide segments comprise the variable and constant domains of the light and heavy chains, respectively, of a single antibody. This embodiment is clearly encompassed by Applicants' election of the variable domain and the constant domain of an antibody

light chain for the first polypeptide segment and a variable domain and a constant domain of an antibody heavy chain for the third polypeptide segment.

Claim 15 recites that the cleavable peptide sequence comprises the sequence of SEQ ID NO:1. Applicants submit that SEQ ID NO:1 is encompassed by the election of a disordered region cleavable by urokinase in the second polypeptide segment as presently elected.

Accordingly, Applicants respectfully submit that claims 7 and 15 read on the elected species.

III. Objection to the Drawings

The Examiner objects to Figure 4A as the reference character "77" has been used to designate both the second polynucleotide and the linker. Applicants have amended the specification to clarify that "77" in Figure 4A refers to the linker and that the second polynucleotide is not shown.

The Examiner further objects to Figures 2, 3A-3B, and 4A-4B because they include reference characters not mentioned in the description. The specification is amended to properly include all the reference characters described in the figures. Further, Figure 4A is amended to properly recite "72" instead of "82" for the first polypeptide segment.

Accordingly, Applicants respectfully request withdrawal of the objections to the Drawings.

IV. Objection to the Specification

The specification is objected to for containing embedded hyperlinks. Applicants have amended the specification to remove the embedded hyperlinks. Accordingly, Applicants respectfully request withdrawal of the objections to the specification.

V. Objection to the Claims

Claim 16 is objected to under 37 C.F.R. § 1.75(c) as failing to further limit the subject matter of a previous claim. Applicants respectfully submit that claim 16 does further limit claim 1. As noted by the Examiner, claim 1 is drawn to a first polypeptide segment, a second polypeptide segment having a cleavable peptide sequence, and a third polypeptide segment. However, claim 1 does not require that neither the first polypeptide nor the third polypeptide segments also include a cleavable peptide sequence as recited in claim 16. As such claim 16 further limits claim 1 and Applicants respectfully request the objection to the claim be withdrawn.

VI. Rejections under 35 U.S.C. §102

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30-31, and 35 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Ladner *et al.* (U.S. Patent No. 5,223,409).

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30, and 35 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Griffiths *et al.* (U.S. Patent No. 5,962,255).

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30-31, and 35 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Wang *et al.* (U.S. Patent No. 6,833,441).

Applicants respectfully traverse these rejections.

A. The Present Invention

The present invention relates to an expression vector for expressing a multimeric polypeptide anchored on a surface of a genetically replicable package formed by a host. The expression vector comprises a vector segment encoding a polypeptide sequence having (i) a first polypeptide segment, (ii) a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent, and (iii) a third polypeptide segment having therein an anchoring peptide sequence for anchoring the multimeric polypeptide to said surface of the

genetically replicable package. The second polypeptide segment is between the first polypeptide segment and the third segment. The cleavable peptide sequence is cleaved by the proteolytic agent, whereby the first segment associates with the third segment to form the multimeric polypeptide.

B. The Cited References

LADNER ET AL. relate to a method of obtaining a nucleic acid encoding a binding protein. In this method, a gene obtained by random mutagenesis of a limited number of codons is fused to a genetic element which causes the resulting chimeric expression product to be displayed on the outer surface of a genetic package (abstract). Genetic variation is achieved through variegation of DNA yielding a mixture of DNA molecules encoding different but related potential binding proteins (see Col. 7, lines 50-54). The hybrid genes comprise a first DNA sequence which encodes a potential binding domain for the target of interest and second DNA sequence which encodes an outer surface protein to display the protein on the outer surface of the package.

GRIFFITHS ET AL. describe a recombinant vector that encodes a first and a second polypeptide component of members of a specific binding pair using recombination between first and second vectors comprising the nucleic acids encoding the sbp members to produce a recombinant vector encoding a first and a second polypeptide chain component of a sbp member.

WANG ET AL. provide techniques for specific assembly of monomeric polypeptides to form a heterodimer.

C. Analysis

According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

1. Rejection over Ladner *et al.*

Ladner *et al.* teach a chimeric protein for display on the outer surface of a genetic package such as a phage. Nowhere do Ladner *et al.* teach a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent as in present claim 1. Instead, Ladner *et al.* teach DNA molecules encoding a chimeric protein comprising a display sequence and a binding domain, where the display sequence directs secretion of the binding domain. The display sequence may comprise both a signal sequence and an outer transport sequence. While the signal sequence may be cleaved, the signal sequence is positioned at a terminal end of the protein and is not "between the first polypeptide segment and the third segment."

2. Rejection over Griffiths *et al.*

Griffiths *et al.* fail to teach a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent as in present claim 1. Instead, Griffiths *et al.* teach recombination of first and second vectors to produce a vector encoding both a first and a second polypeptide chain of a sbp member. Griffiths *et al.* make no mention of a second polypeptide segment having a cleavable peptide sequence therein.

3. Rejection over Wang *et al.*

Wang *et al.* fail to teach a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent as in present claim 1. As described at col. 40, lines 12-13, the vector expresses two proteins rather than a single polypeptide sequence having three polypeptide segments as in the present claims. Wang *et al.* make no mention of a second polypeptide segment having a cleavable peptide sequence therein.

Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102.

VII Rejections under 35 U.S.C. §103

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30-31, and 35 were rejected under 35 U.S.C. §103 as allegedly obvious over Ladner *et al.* and Goers *et al.* (U.S. Patent No. 4,867,973).

Claims 1-4, 6, 11, 13, 16-21, 25-26, 29-31, and 35 were rejected under 35 U.S.C. §103 as allegedly obvious over Griffiths *et al.* and Goers *et al.*

Claims 1-4, 6, 11, 13, 16-21, 25-26, 29-31, and 35 were rejected under 35 U.S.C. §103 as allegedly obvious over Wang *et al.* and Goers *et al.*

These rejections are respectfully traversed.

A. The Present Invention is described above.

B. The Cited References

LADNER ET AL. is described above.

GOERS ET AL. relate to antibody-therapeutic agent conjugates having a therapeutic agent covalently attached to an antibody or antibody fragment.

GRIFFITHS ET AL. is described above.

WANG ET AL. is described above.

C. Analysis

According to the M.P.E.P. § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

1. Rejection over Ladner *et al.* in view of Goers *et al.*

The deficiencies of Ladner *et al.* are discussed above. Nor would one of skill in the art seek to "imbed" the signal peptide between two flanking sequences as the signal sequence would not be expected to direct the post translational transport of the protein, which is the function of the signal sequence. Most signal peptides are located at the N-terminus where they are cleaved by a peptidase subsequent to directing the synthesized proteins.

With regard to claims 2-7, while "Ladner *et al.* teach the display system may be utilized to develop antibodies (please refer to column 15, lines 65-68)," further reading reveals "its primary utility resides in the development of binding proteins which are not antibodies or even variable domains of antibodies" (column 15, line 68 through column 16, line 2. Thus, Ladner *et al.* is not particularly concerned with the difficulties of developing anchored antibodies.

Nor does Goers *et al.* provide the missing teaching as this reference makes no mention of an expression vector for expressing a multimeric polypeptide as presently claimed. Instead, Goers *et al.* is cited merely for a teaching of a urokinase peptide cleavage sequence.

2. Rejection over Griffiths *et al.* in view of Goers *et al.*

The deficiencies of Griffiths *et al.* are discussed above. Nor would one of skill in the art modify Griffiths *et al.* to include a second polypeptide segment having a cleavable peptide sequence as the added sequence would affect folding of the sbp members. Nor is there any guidance for including a second polypeptide segment and addressing the problems associated therewith, which include efficiency of the cleavage and/or purification from the cleavage enzyme.

Nor does the teaching in Goers et al provide the missing teaching. In fact, Goers *et al.* make no mention of an expression vector. Instead, Goers *et al.* is cited merely for teaching a urokinase peptide cleavage sequence.

3. Rejection over Wang *et al.* in view of Goers *et al.*

The deficiencies of Wang *et al.* are discussed above. Nor would one of skill in the art modify Wang *et al.* to include a second polypeptide segment having a cleavable peptide sequence as the proteins are separately produced. Goers *et al.* also fails to make up for this deficiency as the reference makes no mention of an expression vector as presently claimed.

As the references, alone or in combination, fail to teach or suggest all the claim limitations, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted

Date: May 3, 2006

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